Postinfectious Acute Cerebellar Ataxia in Childhood

Çocukluk Çağında Postenfeksiyöz Akut Serebellar Ataksi

Acute Cerebellar Ataxia

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Özet

Amaç: Postenfeksiyöz akut serebellar ataksi çocukluk çağı ataksilerinin en sık sebebidir. Olgular çocuk acil servis veya çocuk nöroloji polikliniklerine ani başlangıçlı ataksi ile başvururlar. Varisella virüsü en sık ilişkilendiren virüstür. Bu çalışmanın amacı postenfeksiyöz akut serebellar ataksi nedeniyle izlenen çocuklarda klinik özellikleri, etiyoloji ve prognozu belirlemek ve çocukluk çağında akut ataksiye genel bir yaklaşım önermektir. Gereç ve Yöntem: Ocak 2011-Haziran 2015 tarihleri arasında başvurmuş 16 çocuğun dosyaları geriye dönük olarak incelendi. Bulgular: Dokuz olgu erkekti (%56,2). Olguların çoğunluğunun yaşı 2-5 yaş aralığındaydı (%62,5). Olguların %87,5'inde bulguların ortaya çıkmasından önce viral enfeksiyon öyküsü mevcuttu: Çocukların ikisinde suçiçeği enfeksiyonu, birinde Epstein Barr enfeksiyonu geri kalanlarda nonspesifik ateşli hastalık saptandı. Ateşli hastalık ve bulguların ortaya çıkışı arasındaki ortalama süre 7,4 (±5) gündü. Ortalama hastane yatış süresi 4,37 (± 1,4) gündü. Ortanca iyileşme süresi 7 gündü. En uzun iyileşme süresi 4 aydı. Tartışma: Çocukluk çağında postenfeksiyöz akut serebellar ataksi, ani başlayan aylar içinde iyileşme gösteren benign bir durumdur. Ancak akut serebellar ataksinin bir dışlama tanısı olduğu unutulmamalı; bu çocuklarda laboratuar testleri ve görüntüleme incelemelerinin uygun kullanımı ile santral sinir sistemi enfeksiyonu ve kitle lezyonu gibi daha ciddi medikal durumların ayırıcı tanısı mutlaka yapılmalıdır.

Anahtar Kelimeler

Postenfeksiyöz Akut Serebellar Ataksi; Çocuk; Serebellit; Varisella Enfeksiyonu; Serebellar Ataksi

Abstract

Aim: Postinfectious acute cerebellar ataxia is the most common cause of childhood ataxia. Cases present with acute onset of ataxia to pediatric emergency and pediatric neurology clinics. Varicella zoster is the most commonly associated virus. The aim of this study is to assess the clinical features, etiology, and prognosis of children with postinfectious acute cerebellar ataxia and to propose a diagnostic approach to acute cerebellar ataxia in children. Material and Method: Files of 16 children admitted between January 2011 and June 2015 were retrospectively evaluated. Results: Nine patients were male (56.2%). The majority of the cases were in the 2-5 years age group (62.5%). A history of a preceding febrile infection was noted in 87.5% of the cases: Two children had varicella infection, one Epstein Barr infection, and the rest nonspecific febrile illness. The mean time interval between the prodromal febrile illness and the onset of the symptoms was 7.4 (±5) days. The mean time of hospitalization was 4.37 (± 1.4) days. The median time for recovery was 7 days. The longest time for recovery was 4 months. Discussion: Postinfectious acute cerebellar ataxia in childhood is the most common cause of childhood ataxia, which presents abruptly and requires recovery over weeks. However, it should be kept in mind that it is a diagnosis of exclusion. Appropriate utilization of laboratory tests and imaging studies is necessary for the differential diagnosis from other serious causes of acute cerebellar ataxia including central nervous system infections and mass lesions.

Keywords

Postinfectious Acute Cerebellar Ataxia; Children; Cerebellitis; Varicella Infection; Cerebellar Ataxia

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Introduction

Acute ataxia is a relatively common presentation to pediatric emergency departments or pediatric neurology clinics. It is characterized by motor incoordination of fewer than 72-hours duration in a previously healthy child and is usually most prominently seen in the child's movements, such as walking and picking up objects. [1]. Acute cerebellar ataxia is the most common cause of acute ataxia in childhood, accounting for 30-50% of all cases [2]. It is characterized by the sudden onset of ataxia following a viral infection, usually varicella [2,3]. However, other infectious agents including Epstein Barr virus (EBV), mumps, Legionella pneumophila, hepatitis A, influenza, herpes simplex, enterovirus, parvovirus B19, rubeola, and mycoplasma pneumoniae are also associated with acute cerebellar ataxia [1,4]. Acute cerebellar ataxia usually results from postinfectious cerebellar demyelination; it less commonly occurs as a result of direct infection of the cerebellum. Postinfectious cerebellar demyelination is thought to be an autoimmune phenomenon incited by infection or immunization [5]. The differential diagnosis of acute cerebellar ataxia is broad. It is a diagnosis of exclusion after other serious conditions including posterior fossa tumors, neuroblastoma (opsoclonus-myoclonus syndrome), acute hemorrhage, drug intoxications, acute labyrinthitis, and metabolic diseases (Hartnup disease, Maple syrup urine disease) have been ruled out [2]. In this study, we aim to analyze all cases of acute cerebellar ataxia presented to our pediatric neurology clinic in order to characterize the clinical features, etiology, and prognosis of the disease and to propose a diagnostic approach to acute ataxia in children.

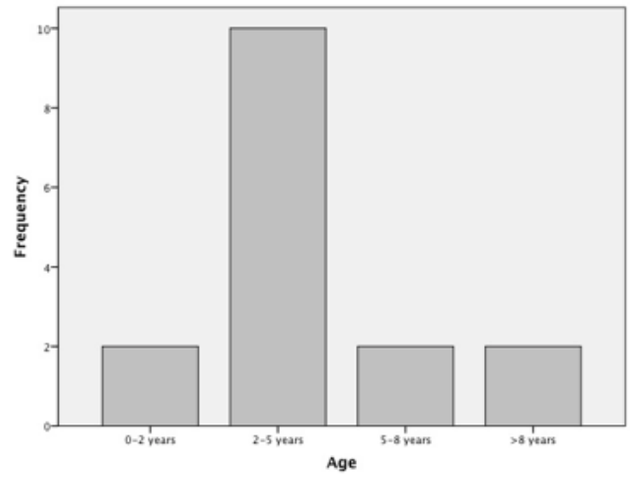
Material and Method

In this descriptive study, the files of the children diagnosed with acute cerebellar ataxia admitted between January 2011 and June 2015 to our pediatric neurology clinic were examined for age, sex, etiology, accompanying neurological findings, laboratory and imaging findings, hospitalization time, healing time and follow-up time after hospital discharge. A total of 16 patients were included in the study. The diagnosis of acute cerebellar ataxia was based on the following criteria: acute-onset loss of coordination or gait difficulties with or without nystagmus, lasting fewer than 72 hours in a previously healthy child, and the absence of known genetic disorders presenting with ataxia, drug intoxication, bacterial meningitis, episodic ataxia syndromes, and metabolic disorders. The local ethics committee approved the study.

Results

The study included 9 males (56.25%). Mean age at presentation was 4.5 years (±3.06). The youngest patient was 1 year of age and the oldest patient was 13. The demographic and clinical characteristics of the patients are presented in Table 1. Ten of the included cases were in the 2-5 year age group (Figure 1). A febrile illness preceded the onset of symptoms in 14 of the cases. This illness was a nonspecific febrile illness in 11 of the cases. Two patients had a preceding varicella infection whereas one patient had a preceding EBV infection. The mean time interval between the prodromal febrile illness and the onset of

Figure 1. The distribution of cases according to age

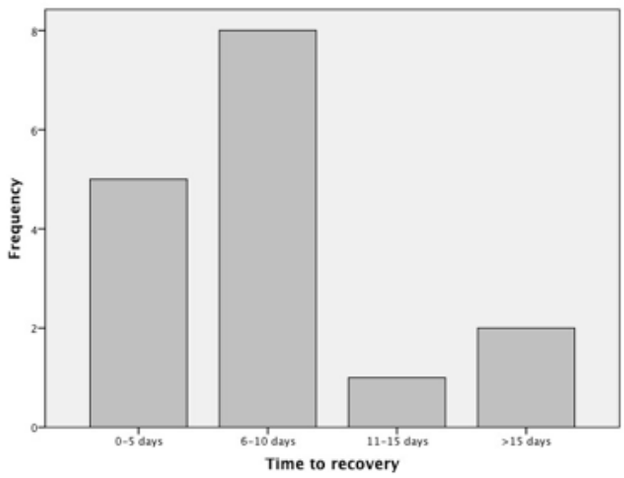


Tablo 1. Demographic and clinical characteristics of the patients

Patient number	Gender	Age	Etiology	Prodrome (days)	Associated neurological Symptoms	Lumbar Puncture Protein levels (mg/dl)	Cranial Imaging	Treatment	Recovery (days)
1	male	2.5	Nonspecific febrile illness	5	-	15,50	MRI	-	7
2	male	3,5	Nonspecific febrile illness	7	dysarthria	14.20	MRI	-	5
3	female	4	Nonspecific febrile illness	2	nystagmus	-	MRI	-	4
4	male	2.5	Nonspecific febrile illness	5	dysarthria, dysmetria	22	MRI	-	7
5	male	1.75	Nonspecific febrile illness	10	-	-	MRI	-	8
6	female	9.5	Nonspecific febrile illness	7	dysarthria	-	MRI	-	21
7	male	5.5	Nonspecific febrile illness	2	nystagmus	-	MRI	-	7
8	female	2	-	-	nystagmus	-	MRI	-	10
9	female	4	EBV	14	-	19	MRI	-	10
10	female	4.5	Nonspecific febrile illness	21	dysmetria	-	MRI	-	7
11	male	2.5	Nonspecific febrile illness	7	dysmetria	24	MRI	IVIG	11
12	male	5.5	Varisella	7	-	21	MRI	-	5
13	female	6	Varisella	7	dysmetria	-	MRI	-	5
14	male	1	Nonspecific febrile illness	3	-	-	CT	-	2
15	female	4.5	Nonspecific febrile illness	7	dysmetria	28	MRI	IVIG	120
16	male	13	-	-	dysmetria	-	MRI	Pulse steroid	10

the symptoms was 7.4 (±5) days. Dysmetria and dysarthria were the most common accompanying neurological symptoms. The median time for recovery was 7 days. Eight patients healed during the 6-10 day interval (Figure 2). The longest time for recovery was 4 months in a 4½-year-old girl. Lumbar puncture was performed in 7 of the cases. Cerebrospinal fluid protein levels were normal in all of the cases, with a mean of 20,8 mg/dl (±4,9). All patients underwent a cranial imaging, 15 underwent brain magnetic resonance imaging (MRI), and one underwent brain computerized tomography (CT). The results were normal in all of the cases. Electromyography (EMG) was performed in 4 of the cases to exclude Guillain Barre Syndrome (GBS). The results did not reveal any pathology. Two patients were treated with intravenous immunoglobulin (IVIG) and one patient was treated with intravenous methylprednisolon because of the severity of the symptoms and the lack of clinical improvement during the hospitalization period. The mean time for hospitalization was 4.4 (±1.4) days. Three patients were lost to follow-up; the mean follow-up time for the rest of the cases was 2.2 (±1,4) months. Full recovery was observed in all of the cases. One case still had minor degrees of gait ataxia and abnormal cerebellar examination in the 2-month follow-up visit; however, these signs had subsided by the 4-month follow-up visit.

Figure 2. The distribution of cases according to time to recovery



Discussion

There is a small number of case series involving acute cerebellar ataxia in the published literature. In 1959, Weiss and Carter [6] described 18 patients with acute cerebellar ataxia. Six of these children had permanent neurological sequelae including gait disturbances and delayed speech development.

Connolly et al [7] reported the evaluation of 73 patients in 1994. Thirty-six of the cases were related to nonspecific viral infections. Varicella infection was responsible for 19 of the cases, EBV for 2. Fourteen cases were found to be idiopathic and 2 secondary to immunization. Cerebrospinal fluid examination revealed pleocytosis and CSF protein levels ranged between 7-99 mg/dl. Nine patients underwent cranial MRI, of which only 1 examination revealed pathology. Ataxia resolved in 91% of the cases after 4 months of follow-up; however 20% of the cases exhibited behavioral problems and learning difficulties, which subsided during follow-up. Recurrence of symptoms was observed in 4 patients.

Nussinovich et al [2] reported a prodromal illness in 29 of the 39 cases in 2003. About one-third of these cases had varicella infection. Mumps, EBV, mycoplasma, and nonspecific infections were noted in the remainder of the cases. Full recovery without any neurological sequelae was achieved within 24 days in all of the cases. A lumbar puncture was performed in all cases. Pleocytosis was present in 48% of the cases and abnormal CSF protein levels (>40 mg/dl) were observed in 23.5%. Twelve patients underwent CT imaging that revealed normal results. The most commonly-associated neurological findings were dysmetria and dysarthria; nystagmus was noted in only 3 of the cases. Electroencephalography (EEG) was performed in 12 cases. Background slowing was observed in 4 of the cases and epileptic discharges without clinical seizures were observed in 2 cases. The authors stated that acute cerebellar ataxia is a self-limiting disease.

In 2006, Martinez-Gonzalez et al. [8] reported a favorable prognosis in 20 cases with acute cerebellar ataxia attributed to varicella, mycoplasma, enterovirus, EBV, and nonspecific viral infections.

Acute cerebellar ataxia is common in children between 2 and 4 years of age, but also may be seen in older children and adolescents (3,7). Boys are more commonly affected [7]. A history of a febrile illness 5-21 days before the first appearance of the symptoms is evident in about 70% of patients. In our study group, there was a slight male preponderance, the incidence of acute cerebellar ataxia was higher in the 2-5 years age group, and a preceding illness accompanied most of the cases. All of these findings were consistent with the literature.

Varicella may be responsible in as many as 26% of the cases; rarely does ataxia occur before the eruptions [1]. Compared with the literature, in our study group, the rate of acute cerebellar ataxia following varicella infection is lower, which may be attributed to the routine use of varicella vaccine after 2012 in our country.

In our series, all of the cases recovered without any neurological sequelae. Only one case had slight gait ataxia and abnormal cerebellar examination after 2 months of discharge; they eventually subsided completely. This case was a 4 1/2 year-old-girl with a severe gait ataxia at onset causing an inability to walk. She was treated with IVIG.

Acute postinfectious cerebellar ataxia is a diagnosis of exclusion. Detailed evaluation with history and physical examination is more valuable than laboratory tests and imaging techniques in the differential diagnosis. An altered state of consciousness, presence of hallucinations, behavioral changes, and a sleepy state should raise the suspicion of drug intoxication. Acute disseminated encephalitis (ADEM) and meningoencephalitis should be on the differential diagnosis list when fever is added to these symptoms [9]. Drug intoxication constitutes about 32.5% of all childhood acute ataxia cases; therefore children and parents should be questioned about drug intake [3]. Anticonvulsant drugs, benzodiazepines, alcohol, and antihistaminic drug intoxication may cause ataxia. Motor examination should be carefully performed because ataxia may be the first sign of hemiparesis or paraparesis in younger children. Posterior circulation infarcts are relatively rare in young children but should

be considered after neck trauma (causing vertebral artery dissection) or in those predisposed to thromboembolic disease [10,11]. Focal cerebral (usually parietal or frontal) and pyramidal tract lesions manifest with a positive Babinski sign and increased deep tendon reflexes [12]. Vomiting and nystagmus should raise the suspicion of labyrinthitis and in the presence of chaotic eye movements, opsoclonus myoclonus syndrome should be considered. Guillain Barre Syndrome should be on the differential diagnosis list when weakness and absence of deep tendon reflexes predominate [9].

Posterior fossa tumors usually present with slowly progressive ataxia and symptoms of increased intracranial pressure such as papilledema and sixth nerve palsy [13]. Brain imaging should be performed in suspected cases. In our study group, all children underwent brain imaging. The results were normal. Although cranial imaging was performed in selected cases in the literature [2,6,7], in countries where patient follow-up is a major problem, it might be more appropriate to evaluate all acute-onset ataxia cases with brain imaging upon admission for the early diagnosis and intervention of brain tumors.

Cerebrospinal fluid examination usually reveals normal results or mild pleocytosis and slight elevation of protein levels. Lumbar puncture should only be performed when central nervous system (CNS) infection is suspected [3]. Rarely, an LP may be helpful in differential diagnosis from GBS, when EMG is not available. However it should always be kept in mind that the CSF protein levels may be normal during the first week of GBS [14]. Therefore an LP is generally not indicated at the initial presentation of acute ataxia [1].

Electromyography is indicated when GBS is considered in the differential diagnosis. We performed EMG on only 4 patients. None of the patients underwent EEG because an altered state of consciousness was not observed in any of them.

Opsoclonus-myoclonus syndrome is a rare autoimmune condition mostly associated with neuroblastoma in childhood [15]. Thorax and abdomen CT or MRI or I123 metaiodobenzilguanidin (MIBG) scanning might be helpful for diagnosis of neuroblastoma in these patients because the levels of cathecolamines in the urine are increased in only 47-60% of the cases [16,17,18].

The treatment of acute cerebellar ataxia is usually watchful waiting; physiotherapy may be helpful in selected cases [15]. Since an autoimmune process has been suggested in the etiology, high dose corticosteroids and IVIG has been used in treatment with favorable results [19,20]. However, the results are mostly limited to case reports and the yield of corticosteroid and IVIG therapy is uncertain (1). We tried IVIG in 2 patients and high dose corticosteroids in 1 patient because of a severe and resistant course without an evident clinical response. Recovery usually begins within the first week after the onset of symptoms [1]. The average duration of symptoms is about 2 months; ataxia remains persistent in a small group of patients [7].

In conclusion, postinfectious acute cerebellar ataxia is the most common cause of acute ataxia in childhood. The prognosis is excellent; however, it causes great anxiety to the parents. After the exclusion of more serious medical conditions presenting with acute ataxia, informing the parents about the course of the disease and close follow-up during recovery is necessary.

Competing interests

The authors declare that they have no competing interests.

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